UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,586	12/12/2005	Gabriele Multhoff	KNAUTHE-09734	3810

72960 7590 03/21/2008

Casimir Jones, S.C.
440 Science Drive
Suite 203
Madison, WI 53711

EXAMINER	
KOSAR, ANDREW D	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
03/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,586	MULTHOFF, GABRIELE	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 25-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 25-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 12, 2007 has been entered.

Response to Amendments/Arguments

Applicant's amendments and arguments filed December 12, 2007 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below in original or modified form is herein withdrawn.

Applicant argues that the amendments to the claims distinguish over the prior art, asserting that the recitation of "isolated granzyme B as the only pharmaceutically active component" does not allow for the prodrug delivery peptide. Applicant argues that the delivery peptide is an "additional active component" (Remarks, page 2), and asserts that prodrug forms are now excluded by the claim language. Applicant further argues that the prior art does not teach Hsp70 expressing cells, and thus are not anticipated. With regards to the obviousness rejection, Applicant argues that Trouet teaches away requiring an additional active agent (the delivery peptide), thus the claims are not obvious.

Respectfully, the examiner disagrees. A delivery peptide as the prodrug form is not the same as a second active agent, as Applicant would assert. A second active agent would be considered to be another compound that functions in the same way as the granzyme B peptide,

e.g. a compound that induces apoptosis. In contrast, a delivery peptide coupled as a prodrug to the granzyme is not an active agent, but rather a means to deliver the active agent. Here, Applicant has amended the claims to exclude coadministration of other compounds that function as granzyme B, and not delivery as a prodrug. Additionally, in making the prodrug form, one necessarily starts with 'isolated granzyme B', as required by the claims, and thus the claims are still anticipated and rendered obvious by the prior art. Furthermore, one would not consider the protective nature of a prodrug (reducing proteolysis, etc.) to be equivalent to a second active agent.

Double Patenting

Applicant is advised that should claims 17 and 25-28 be found allowable, claims 29-33 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 17, 28 and 29 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by TROUET (WO 01/91798 A1).

The instant claims are drawn generally to administration of granzyme B to a human to treat viral or bacterial infection, inflammatory diseases or a tumor.

Trouet teaches granzyme B induces apoptosis(e.g. page 31) and is conjugated to a delivery peptide as a "tumor specific prodrug formulation" (e.g. Example 14, page 53), further teaching pharmaceutical compositions (e.g. claim 56) and the method of inhibiting tumor growth *in vivo*, *ex vivo* or *in vitro* with the prodrugs of Trouet (e.g. claim 53). Trouet teaches how one would determine effective dosages for practicing the methods (e.g. Page 39, *5.9.2 Effective Dosages*).

Here, Trouet does not distinguish the type of tumor cell, and thus embraces all tumor cells, including those expressing Hsp70 on the surface. Furthermore, nothing in Trouet precludes administration to cells expressing Hsp70. Additionally, the limitations of steps (b) and (c) are *in vivo* and cannot be controlled by the administration of the drug, and thus would inherently occur when granzyme B is administered as in the method of Trouet. Further, as discussed previously, claim 28, and now new claim 33, do not require selection of 'viral infection', and merely limits the Markush group to a subset (e.g. claim 17 is A, B or C, claim 28 is A, B' or C), and thus properly is rejected as reading upon tumor.

With regards Trouet teaching a prodrug form, the instant claim does not exclude such prodrug forms, as the instant claims requires administration of a pharmaceutically effective amount of isolated granzyme B and administration of the prodrug form of Trouet delivers a pharmaceutically effective amount of granzyme B. Here, the prodrug form is merely considered a means to deliver the peptide to the cell, acting as a carrier, and does not materially change the fact that it delivers a pharmaceutically effective amount of granzyme B.

Claims 17, 28 and 29 are/remain rejected under 35 U.S.C. 102(e) as being anticipated by TROUET (II) (Previously cited as US 2004/0014652 A1; PTO-892, 3/6/07). Trouet (II) is the National Stage Application of Trouet, *supra*.

The instant claims are presented *supra*.

Trouet (II) teach Granzyme B as an agent for treatment of tumors and cancers (paragraphs [0013], [0139], [0140-0141], and [0277-0281]) and claim Granzyme B as an agent in compositions for treating cancer cells in claims 29, 35, and 51. Trouet (II) discloses the addition of a masking or protecting moiety to Granzyme B, among other agents of interest, in order to give it more protection from proteases and peptidases present in the circulatory system as well as allowing it to penetrate the nuclear membrane more readily once it is in the cell. Trouet teaches that therapeutically effective and safely tolerated amounts of the compositions should be used (paragraph [0189]), and do broadly teach how to use findings from cell culture and animal studies to determine safe and effective doses and dosing schedules suitable to the organism, disease and agent being used (e.g. paragraph [0184] and [0205]).

Here, Trouet does not distinguish the type of tumor cell, and thus embraces all tumor cells, including those expressing Hsp70 on the surface. Furthermore, nothing in Trouet precludes administration to cells expressing Hsp70, teaching broadly administering to any tumor. Additionally, the limitations of steps (b) and (c) are *in vivo* and cannot be controlled by the administration of the drug, and thus would inherently occur when granzyme B is administered as in the method of Trouet. Further, it is noted that claim 28 and 33 do not require selection of 'viral infection', and merely limits the Markush group to a subset (e.g. claim 17 is A, B or C, claim 28 is A, B' or C), and thus properly is rejected as reading upon tumor.

With regards Trouet teaching a prodrug form, the instant claim does not exclude such prodrug forms, as the instant claims requires administration of a pharmaceutically effective amount of isolated granzyme B as the sole active component, and administration of the prodrug form of Trouet delivers a pharmaceutically effective amount of isolated granzyme B. Here, the prodrug form is merely considered a means to deliver the peptide to the cell and does not materially change the fact that it delivers a pharmaceutically effective amount of granzyme B, acting as a carrier of the peptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17 and 25-33 are/remain rejected under 35 U.S.C. 103(a) as being unpatentable over TROUET or TROUET (II). Trouet and Trouet (II) are discussed together as they have the same disclosure and teachings.

The instant claims and teachings of Trouet and Trouet (II) are presented *supra*. The instant claims are further drawn to the granzyme B being adminsiterd at various final concentrations, e.g. about 6 ng/ml.

Trouet and Trouet (II) each teach administration of granzyme B to treat/inhibit growth of tumors and means by which one could determine the effective dosages to administer, as discussed above.

Trouet and Trouet (II) are each relied upon for the reasons discussed above. If not expressly taught, based upon the overall beneficial teaching provided by this reference with respect to making dosages and determination of the effective dosages, in the manner disclosed therein, the adjustments of particular conventional working conditions (e.g., determining one or more suitable dosage ranges of granzyme B to administer), is deemed merely a matter of judicious selection and routine optimization, as it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. final concentration of granzyme B adminsitered), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05), and such selection and optimization is well within the purview of the skilled artisan.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

References cited on the attached PTO-892 are made of record, but not relied upon and are considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654